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Facile synthesis of the cyclopentane moiety of (all-*E*,2*R*,5*R*,6*S*)-2,6-cyclolycopene-1,5-diol

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Abstract

The carotenoid (2*R*,5*R*,6*S*)-2,6-cyclolycopene-1,5-diol (**1**) bears a tetrasubstituted cyclopentane ring with three neighbouring stereogenic centers. The cyclic aldehyde **2** with the correct substitution pattern was synthesized in four steps from (*R*)-α-terpineol (**3**). From **2** the carotenoid **1** was prepared and investigated by CD spectroscopy.

Keywords: terpene; carotenoid; aldol addition.

Numerous terpenes and derivatives thereof serve as cheap and readily available starting materials in chemical synthesis. In contrast to its six-membered analogues, cyclopentane building blocks are scarce. We report here on the synthesis of a tetrasubstituted cyclopentane derivative which was used in the course of our studies on the total synthesis of optically active (all-*E*,2*R*,5*R*,6*S*)-2,6-cyclolycopene-1,5-diol (**1**),[1] which possesses anticancer activities against prostate cancer.[2] The preparation of racemic **1** has been reported earlier[3] (Fig. 1).

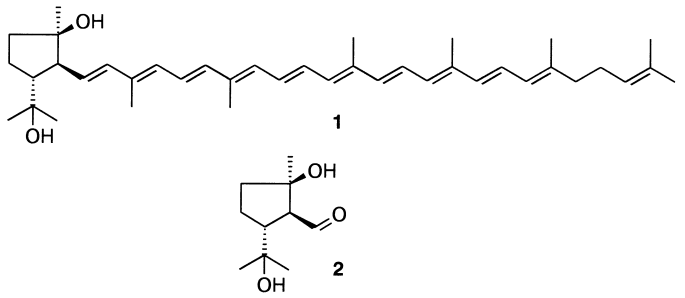

Figure 1.

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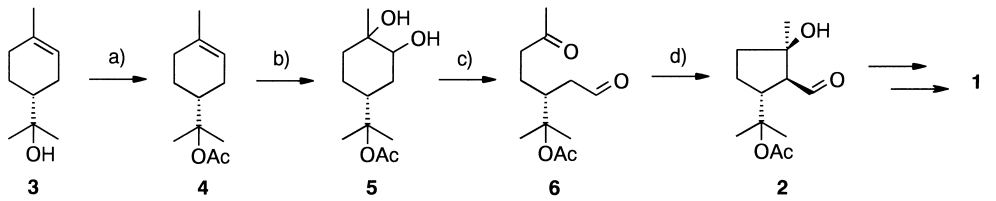
(*R*)-α-Terpineol (**3**) was acetylated with acetic anhydride, 4-dimethylaminopyridine and triethylamine to (*R*)-α-terpinyl acetate (**4**) and dihydroxylated with potassium permanganate to give **5**. Oxidative cleavage with lead tetraacetate to **6** and cyclization by an intramolecular aldol addition, catalyzed by acetic acid and piperidine gave the cyclic aldehyde **2** (Scheme 1). NMR studies show the carbaldehyde function to be *trans* to the substituent at C(3) and *cis* to the hydroxy group at C(1).



Scheme 1. Synthesis of (1*R*,2*S*,3*R*)-**2** and (all-*E*,2*R*,5*R*,6*S*)-**1**. Reagents and conditions. (a) Ac_2O, DMAP, NEt_3, pyridine, rt; (b) $KMnO_4$, THF/H_2O, 0°C; (c) $Pb(OAc)_4$, Na_2CO_3, CH_2Cl_2, 0°C; (d) piperidine, AcOH, H_2O, THF, rt

(all-*E*,2*R*,5*R*,6*S*)-2,6-Cyclolycopene-1,5-diol (**1**) was prepared from **2** as reported in Ref. 3 for the racemic compound. The CD spectrum (EPA, –180°C) shows relative maxima at 228, 297.5, 455, 498 and 515.5 nm and relative minima at 214.5, 244, 283.5, 443.5, 469 and 504 nm in a spectrum close to conservative in type.

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